Extended follow-up of breast cancer patients in clinic wastes time for both patients and doctors: the case against

Short communication

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Much of the debate about the worth, or otherwise, of clinical follow-up of patients after completion of their local and adjuvant therapy for early breast cancer centres around the possible survival benefits of this approach. The limited data, well reviewed by Collins and coworkers [1], do not demonstrate any survival advantage for follow-up. However, those authors identified only five randomized trials addressing follow-up questions, which between them contained 3,116 patients, and so they cannot exclude absolute survival benefits of perhaps 4% or 5% for follow-up strategies. Death, like birth and taxes, remains inevitable in life, and extension of the duration of life justifies only some of what we do in the treatment of breast cancer. For patients with early breast cancer that can be treated by breast conservation, there remains no evidence that this approach offers better survival than mastectomy, but few - if any - would argue against offering women breast conservation. Similarly, more than 6,000 patients were randomized in the ATAC (Arimidex, Tamoxifen Alone or in Combination) adjuvant trial [2], which compared anastrazole with tamoxifen in postmenopausal women with early, hormone receptor positive breast cancer, but there was not even a hint of a survival advantage at over 5 years of follow-up for the use of anastrazole rather than tamoxifen, but it is a widely accepted as an appropriate treatment.

So, if we do not do clinical follow-up to improve survival, what other advantages might there be, and what do accepted guidelines suggest should be done?

Aiming at a North American audience, the American Society for Clinical Oncology (ASCO) guidelines [3] state that, 'The evidence supports regular history, physical examination, and mammography as the cornerstone of appropriate breast cancer follow-up. Examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter. For those who have undergone breast-conserving surgery, a post-treatment mammogram should be obtained 1 year after the initial mammogram and at least 6 months after completion of radiation therapy. Thereafter, unless otherwise indicated, a yearly mammographic evaluation should be performed. The use of [lots of tests] is not recommended for routine breast cancer follow-up in an otherwise asymptomatic patient with no specific findings on clinical examination.'

However, in the UK, the National Institute for Health and Clinical Excellence (NICE) [4], presumably reviewing the same data, concluded that, 'Guidelines for limited (two or three years) follow-up should be agreed by each network. The aims of follow-up should be to detect and treat local recurrence and adverse effects of therapy, particularly lymphoedema. Intensive follow-up, designed to detect metastatic disease before symptoms develop, is not beneficial and should not be provided.'

The only thing both guidelines seem to agree on is the futility of conducting lots of intensive tests to try to detect asymptomatic metastatic disease. What data are there to support the NICE-endorsed limitation of follow-up to only 2 or 3 years, and to focus primarily on lymphoedema as the key toxicity? Data from a retrospective analysis of 1,312 women treated with breast conservation in Edinburgh between 1991 and 1998 suggested that only half of the 'treatable recurrences' were detected mammographically [5]. Furthermore, that same study reported that although the peak incidence of metastatic disease (the one thing that NICE does not think we should be looking for in follow-up clinics) was in the first 2 or 3 years, the risk for local ('treatable') relapse was constant for at least the first 10 years! It would therefore seem that the NICE guidance is inconsistent with this study and much of the rest of the literature, in the sense that limiting follow-up to the first 2 or 3 years does not appear to maximize the chances of detecting and treating local recurrence, with no data to support this recommendation

ASCO = American Society of Clinical Oncology; NICE = National Institute for Health and Clinical Excellence.

Table 1

Summary of follow-up issues and evidence

Follow-up issues	Summary of evidence
Survival advantage	None reported but literature relatively underpowered
Doing no follow-up	Never been tested in a randomized trial
ASCO guidance [3]	Recommendations have not been tested in randomized controlled trials
NICE guidance [4]	No evidence provided for the recommended limit of follow-up to 2 to 3 years
	Local recurrence risk maintained for much longer than recommended follow-up period
Primary care follow-up	Seems acceptable and good, but small trial (<300 patients) [7,8]
	General practitioners needed training, and consultations take more time!
Telephone contact	Some evidence from an unpublished small regional UK trial [15]
Nurses	Acceptable to patients - not necessarily much cheaper
Nonpatient benefits	Audit, research, measuring quality of service, identification of unexpected toxicities of new drugs

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provided in the paper summarizing the evidence base for the 2002 NICE recommendations!

Several authors have reviewed all of the data relating to follow-up [1-6], but few have commented on one critical fact. There is no doubt that the survival of women with early breast cancer is improving. Furthermore, although there is debate as to the relative contributions of screening, better preoperative diagnostics, better local treatments and pathological assessments, and the application of adjuvant therapies, it must be recalled that all of the important studies were based on the assumption that there would be regular and sustained clinical follow-up. Furthermore, all of the randomized trials that compare alternative methods of follow-up have included some form of clinical follow-up in both arms. We therefore ignore this consistent factor in all of those trials at our peril, in the absence of any robust data indicating that follow-up is not important in the treatment of our patients!

Thus, the question to be addressed is not really whether there is any evidence to support ceasing clinical follow-up - there is none. Until such a time that there is a properly powered randomized trial that proves that there is no benefit to patients from being reviewed clinically on a regular basis, we have no evidence to stop doing what most of us, and most of our patients, feel is appropriate - keeping in regular clinical contact. However, the devil is in the detail, and the debate really must focus around how patients can be followed up, how frequently, for how long and what might be the purpose of any follow-up. Table 1 summarises the issues.

Follow-up models

The traditional model is of frequent attendance at busy clinics, usually with a consultant present; the reality, though, is that patients are seen by frequently rotating junior staff. This is reflected in data indicating that patients attending hospital clinics see a median of 10 different doctors over 5 years of follow-up. Could this be better delivered in the primary care sector? One trial randomized 296 patients between follow-up in hospital or by specially trained general practitioners [7,8]. No difference was found in time to diagnosis of relapse or in quality of life, but the investigators did report that patients being followed up in general practice had more, and longer, visits than those in the secondary care sector, but were more satisfied [7,8]. A subsequent, larger study yielded similar findings [9]. A further study compared different frequencies of follow-up and found that less frequent follow-up was preferred by the majority of patients [10].

Should patients undergo regular mammography as part of their follow-up? This is the recommendation of the ASCO guidelines but not of the previous NICE guidelines. The Ontario guidelines recognize that although there are no randomized data to support this approach, there is reasonable level C evidence to support its use to detect both ipsilateral recurrence and contralateral second primary breast cancer [11]. Organizing such regular mammography does not need regular clinic visits but, unless for example it is done within a systematic national breast screening programme, few health care systems are currently in a position to provide this service for breast cancer patients without being based within a clinical structure.

So what sort of follow-up approach does make sense? Montgomery and coworkers [12] reviewed the literature available up to 2006 and concluded that, 'There are no randomised trials in the literature with sufficient power to recommend an acceptable frequency or duration of follow up. Moreover, there are no randomised trials that can confirm the safety of using alternative follow-up methods.' In essence,

they conclude that there is no real evidence for or against any particular follow-up strategy. The NICE guidelines strongly recommend indefinite access to a breast care nurse and that issues of hormonal drug therapy should be left to general practitioners. However, one study reported that up to 15% of patients return to hospital-based clinics within a year of discharge [13], so perhaps this non-clinic-based approach to managing ongoing symptoms is not appropriate for all patients! There are two studies that reported high levels of patient satisfaction with a structured, prebooked, trained nurse led telephone follow-up, combined with CA125 testing in ovarian cancer [14] and with mammography in breast cancer [15]. Thus, it may be that future provision of follow-up will involve more use of technology and nurses, although the latter are not necessarily much more economical than involving junior doctors in the clinic!

A further consideration is the possible benefit for the health care provider of follow-up, which will not be measured in most studies. How can treating clinicians assess the quality of their care, measure medium-term and long-term disease outcome, cosmesis, satisfaction and toxicity of treatment without being able to continue to assess the patients they have treated? How can those planning health care provision be sure that they are delivering optimal service if the outcomes are unknown? What opportunity does discharge to untrained general practitioner offer patients and their relatives to discuss the finer details of their treatment, its toxicities, and all of the implications to them and their families of a diagnosis of breast cancer?

Finally, even NICE recognizes the importance of follow-up for research protocols. At present in the UK, one patient is enrolled to a study in breast cancer for every three or four diagnosed with the disease, and so cessation of regular follow-up for all but those included in trials will have less impact on overall workload than is perhaps anticipated by those health economists who recommend it! Furthermore, as we move into an era of newer therapies, there may be unexpected rare toxicities that will not be detected in a modestly sized trial population, but only in larger national datasets.

Conclusion

Our entire current evidence base for treating breast cancer includes regular, sustained follow-up, and there are no data that provide firm support for any particular level or method of follow-up. Thus, the debate must be about how, where and by whom follow-up should occur, and not about its worthlessness, until such time as a properly powered prospective trial produces evidence to suggest that it is not worth doing from any perspective!

Competing interests

The author declares that they have no competing interests.

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